PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	Richard G. Langlois et al.	Docket No. :	IL-11052
Serial No. :	10/643,797	Art Unit :	1641
Filed :	08/19/2003	Examiner :	Nelson C. Yang
For :	SYSTEM FOR AUTONOMOUS MONITORING OF BIOAGENTS		

Honorable Commissioner for Patents
Alexandria, VA 22313-1450

Attention: Board of Patent Appeals and Interferences

Dear Sir:

APPELLANTS' BRIEF (37 C.F.R. § 1.192)

This brief is submitted in support of Appellants' notice of appeal from the decision of the Examiner, mailed April 29, 2008 rejecting claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 of the subject application. Appellants' filed an earlier Appeal Brief on January 22, 2008. The decision of the Examiner mailed April 29, 2008 is, at least in part, a response to the earlier Appeal Brief. Note the statement in numbered paragraph 30 on page 11 of the decision of the Examiner mailed April 29, 2008: "Applicant may wish to continue with the filing of the appeal brief in response to this office action." Appellants' do wish to continue with the filing of the Appeal Brief.

Appellants' notice of appeal was mailed July 24, 2008.

One copy of the brief is being transmitted per 37 C.F.R. § 41.37.

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I. REAL PARTY IN INTEREST

The real party in interest is:

Lawrence Livermore National Security, LLC and the United States of America as represented by the United States Department of Energy (DOE) by virtue of an assignment by the inventor as duly recorded in the Assignment Branch of the U.S. Patent and Trademark Office.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

III. STATUS OF CLAIMS

The application as originally filed contained claims 1-50.

The claims on appeal are claims 1-5, 12, 15-16, 19, 27, 29, and 31-40.

The status of all the claims in the proceeding (*e.g.*, rejected, allowed or confirmed, withdrawn, objected to, canceled) is:

Claims 41-50 are withdrawn from consideration.

Claims 6-11, 13-14, 17-18, 20-26, 28, and 30 are cancelled.

Claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 are rejected.

Claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 on appeal are reproduced in the Appendix.

IV. STATUS OF AMENDMENTS

There have been no amendments filed subsequent to the Rejection mailed April 29, 2008.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Appellants' invention provides a system for monitoring air for bioagents. Portions of Appellants' specification are quoted and the quote is identified by the page and line numbers.

At present there are more than 30 pathogens and toxins on various agency threat lists. Public health personnel rarely see most of the pathogens so they have difficulty identifying them quickly. In addition, many pathogenic infections aren't immediately symptomatic, with delays as long as several days, limiting options to control the disease and treat the patients. The lack of a practical monitoring network capable of rapidly detecting and identifying multiple pathogens or toxins on current threat lists translates into a major deficiency in the United States ability to counter biological terrorism. (Page 11, lines 18-19 and Page 12, lines 1-6)

In Appellants' invention particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected. Any bioagents in the collected particles are detected by a detector system. (Page 6, lines 7-10) Appellants' invention is illustrated in FIGS. 6, 11, 13, below.

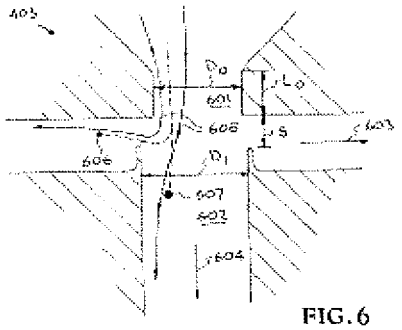
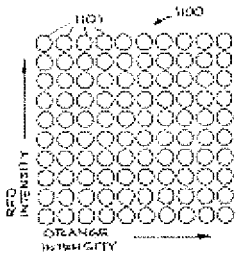


FIG. 6



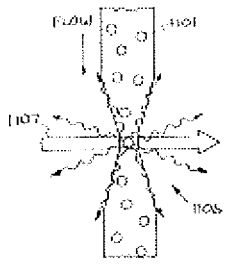


FIG. 13

Small diameter polystyrene beads are coded with 1000s of antibodies. The sample is first exposed to the beads and the bioagent, if present, is bound to the

bead. A second, fluorescently labeled antibody is then added to the sample resulting in a highly fluorescent target for flow analysis. Since the assay is performed on a microbead matrix, it is possible to measure all types of pathogens, including viruses and toxins. Each microbead is colored with a unique combination of red and orange emitting dyes. The number of agents that can be detected from a single sample is limited only by the number of colored bead sets. The system includes the following components: microbead specific reagents, incubation/mixing chambers, a microbead capture array, and an optical measurement and decoding system. (Page 41, lines 17-19 and Page 41, lines 1-8)

There exists a critical need to develop distributed biothreat agent sensor networks that can operate in civilian applications. To operate in "Detect to Protect/Warn" type detection architectures, these platforms need to have several key properties. They need to be capable of detecting pathogens within a 1-2 hour time window, allowing for enough time to respond to an event. They need to be extremely low cost to maintain, since continuous monitoring is essential for many applications. These platforms need to have sufficient sensitivity to cover a broad geographical area (limiting the necessary number of sensors) and have sufficient selectivity to virtually eliminate false positives. (Page 1, lines 17-19 and Page 2, lines 1-9)

Applicants' invention provides an Autonomous Pathogen Detection System (APDS) for monitoring the environment to protect the public from the release of hazardous biological agents. The Autonomous Pathogen Detection System is a countermeasure to bioterrorism, one of the most serious threats to the safety of United States citizens, citizens of other countries, and the military. There is one (1) independent claim, claim 1, involved in the appeal. Appellants' independent claim involved in the appeal is "read on" Appellants' original specification.

Claim 1	Specification & Drawings
1. An autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles, comprising:	The present invention provides a system for monitoring air for bioagents. Particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected. (Page 6, lines 7-9)
a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air;	an aerosol collector system continuously samples the air and traps particles in a swirling buffer solution. Particles of a given size distribution are selected by varying the flow rate across a virtual impactor unit. (Page 21, lines 5-8)
a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles; and	... the collector includes a wetted-wall cyclone collector that receives product air flow and traps and concentrates potential bioagent particles of a predetermined particle size range in a liquid. (Page 7, lines 13-15) The beads are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of one hundred beads, each with a unique spectral address. Each bead 1101 is coated with capture antibodies specific for a given antigen as illustrated in FIG. 12. (Page 44, lines 11-14)
a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads and	A detector for detecting the bioagents in the sample is operatively connected to the sample preparation means. (Page 6, lines 18-19)

Claim 1 (Continued)	Specification & Drawings
wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents.	The APDS 300 integrates a flow cytometer and PCR detector (Page 19, line 5) Each optically encoded and fluorescently labeled microbead is individually read in a flow cytometer, and fluorescent intensities are then correlated with bioagent concentrations. (Page 19, line 5)

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The Rejection mailed April 29, 2008 states four grounds of rejection. The four grounds of rejection are summarized as follows:

Grounds of Rejection #1 – Claim 19 was rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The rejection is stated in numbered paragraph 5 on page 2 of the Rejection mailed April 29, 2008.

Grounds of Rejection #2 - Claims 1-4, 12, 27, 29, 31-35, and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Miles et al US 6,576,459 (hereinafter "Miles") in view of Casey et al US 2002/0187470 (hereinafter "Casey") and in view of Irving et al US 6,468,330 (hereinafter "Irving"). The rejection is stated in numbered paragraphs 7-18 on pages 3-6 of the Rejection mailed April 29, 2008.

Grounds of Rejection #3 – Claim19 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Miles in view of Casey and in view of Irving and further in view of Colston, Jr. et al US 2003/0032172 (hereinafter "Colston"). The rejection is stated in numbered paragraph 19 on pages 6-7 of the Rejection mailed April 29, 2008.

Grounds of Rejection #4 - Claims 1-5, 29, 32, 33, and 35-37 were rejected are rejected under 35 U.S.C. § 103(a) as being unpatentable over Daugherty et al US 2004/0028561 (hereinafter Daugherty) in view of Casey and Irving. The rejection is stated in numbered paragraphs 20-29 on pages 7-10 of the Rejection mailed April 29, 2008.

VII. ARGUMENT

Argument Relating to Grounds of Rejection #1 - Appellants' claim 19 complies with the written description requirement. It is clear from Appellants' original specification that a person skilled in the art would recognize that the inventor(s) had possession of the claimed invention including the claim limitation of claim 19, "wherein said wetted wall sample preparer includes a super serpentine reactor."

Appellants' claim 1 includes the claim element, "a wetted wall sample preparer." Appellants' claim 19 specifies, "The apparatus of claim 1 wherein said wetted wall sample preparer includes a super serpentine reactor."

Presumption of Adequate Written Description

There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). Any implication from the statement in the Rejection mailed April 29, 2008:

> "While applicant do teach a mixing means that is a super serpentine reactor, there is not indication that this is part of the wetted wall sample preparer"

is contradicted by Appellants' specification taken as a whole. Any implication in the Rejection mailed April 29, 2008 is not sufficient to overcome the presumption that an adequate written description of the claimed invention is present when Appellants' filed the application.

Appellants' Specification Supports Claim Limitation

Appellants' specification taken as a whole supports the claim limitation "wherein said wetted wall sample preparer includes a super serpentine reactor." MPEP § 2163 II.A.3 states, "An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying

characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention."

Appellants' specification in paragraph [0072] with reference to FIG. 10 describes the "super serpentine reactor" as - - The means 1003 for mixing the sample and the reagent can be, for example, a super serpentine reactor, available from Global FIA, Inc, Fox Island, WA - -.

Appellants' specification in paragraph [0096] with reference to FIG. 15 describes the "super serpentine reactor" as - - The means 1503 for mixing the sample and the reagent can be, for example, a super serpentine reactor, available from Global FIA, Inc, Fox Island, WA - -.

Inventor(s) Had Possession of Claimed Invention

A person skilled in the art would recognize that the inventor had possession of the claimed invention including the claim limitation "wherein said wetted wall sample preparer includes a super serpentine reactor." of claim 19. The concept and fundamentals of "a super serpentine reactor" were well known in the prior art at the time Appellants filed their patent application which includes the statement, "for example, a super serpentine reactor, available from Global FIA, Inc, Fox Island, WA."

Person Skilled In The Art

The level of skill of a person skilled in the relevant art is very high and they would recognize that the inventor had possession of the claimed invention including the claim limitation "wherein said wetted wall sample preparer includes a super serpentine reactor." It includes scientists with BS degrees in engineering or chemistry and advanced degrees in engineering or chemistry. The inventors are scientists at the Lawrence Livermore National Laboratory. The Lawrence Livermore National Laboratory (LLNL) is a premier applied science laboratory that is part of the National Nuclear Security Administration (NNSA)

within the Department of Energy (DOE). The LLNL website states that LLNL has an annual budget of about US$1.5 billion and a staff of roughly 7,000 employees. The *Wikipedia, the free encyclopedia* describes the Lawrence Livermore National Laboratory. A copy of the *Wikipedia, the free encyclopedia* description of the Lawrence Livermore National Laboratory is provided in the EVIDENCE APPENDIX (IX).

Written Description Rejection Should Be Reversed

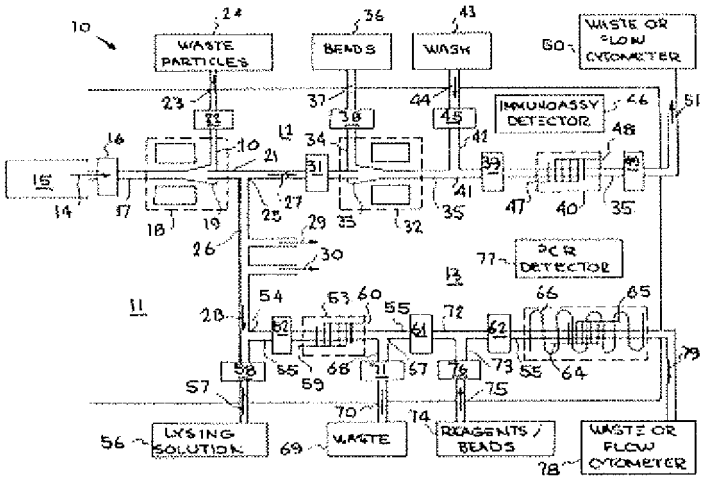
The rejection of claim 19 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement should be reversed.

Argument Relating to Grounds of Rejection #2

The rejection of Appellants' claims 1-4, 12, 27, 29, 31-35, and 40 as obvious over Miles in view of Casey and Irving does not meet the standard of 35 U.S.C. § 103(a).

The Miles Reference

The Miles reference is United States Patent No. 6,576,459 for a sample preparation and detection device for infectious agents illustrated in the figure and portion of specification of the patent reproduced below.



"The sample preparation and detection device comprises a system or device generally indication at 10 located on a single compact, field-portable microchip 11 and includes an immunoassay section 12 and a PCR assay section 13. Sample containing pathogenic particles indicated by arrow 14 is moved from a collector or other source 15 by an MHD pump 16 through a microchannel 17 into an ultrasonic fractionation or filtering assembly generally indicated at 18 and which is sensitive to density and size differences between particles. Microchannel 17 terminates in a separator 19 with microchannels 20 and 21 extending from separator 19. Microchannel 20 is directed through a MHD pump 22 and carries large particles and dense particles indicated by arrow 23, which are transferred to waste as indicated at 24. Microchannel 21 includes a function 25 from which extends a microchannel 26, with microchannel 21 supplying sample to immunoassay section 12 as indicated by arrow 27 and microchannel 26 supplying sample to PCR assay section 13 for DNA analysis, as indicated by arrow 28."

Appellants Disagree with Examiner's Finding of Fact – Miles Reference

The Appellants disagree with the Examiner's Finding of Fact regarding the Miles reference. The Rejection mailed April 29, 2008 states: "Miles et al fail to teach that the use of optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads, each with a unique spectral address and coated with capture antibodies specific for a given antigen, and also fails to teach a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles connected to said collector."

Appellants point out that there are other claim limitations that are not taught by the Miles reference. The Miles reference does not show Appellants' "autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles." The Miles reference only shows a "sample preparation and detection device comprises a system or device generally indication at 10 located on a single compact, field-portable microchip." The Miles reference does not show an autonomous monitoring apparatus for monitoring air for bioagents.

The Miles reference does not show Appellants' "collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air." The Miles reference only shows a "collector or other source 15." The Miles reference does not show a collector separating selected potential bioagent particles from air.

The Miles reference does not show Appellants' "wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid." The Miles reference only shows a "collector or other source 15." The Miles reference does not show a "wetted wall sample preparer" or a "wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector" or a "wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid."

The Miles reference does not show Appellants' "detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads." The Miles reference only shows "immunoassay detector 46" and "PCR detector 77." The Miles reference does not show a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads.

The Miles reference does not show Appellants' "flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a

unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents." The Miles reference only shows a "immunoassay detector 46" and "PCR detector 77." The Miles reference does not show a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents.

The Casey et al Reference

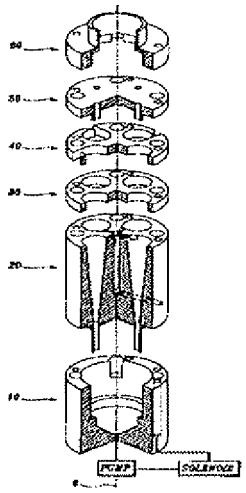
The Casey et al reference is United States Published Patent Application No. 2002/0187470 disclosing methods for rapid detection of single nucleotide polymorphisms (SNPs) in a nucleic acid sample. The Casey et al reference discloses the following method:

> "a method of determining a selected nucleotide polymorphism in genomic DNA treated to reduce viscosity comprising (a) performing an amplification of the genomic DNA using a first nucleic acid primer comprising a region complementary to a section of one strand of the nucleic acid that is 5' of the selected nucleotide, and a second nucleic acid primer complimentary to a section of the opposite strand of the nucleic acid downstream of the selected nucleotide, under conditions for specific amplification of the region of the selected nucleotide between the two primers, to form a PCR product; (b) contacting the PCR product with a first nucleic acid linked at its 5' end to a detectably tagged mobile solid support, wherein the first nucleic acid comprises a region complementary to a section of one strand of the PCR product that is directly 5' of and adjacent to the selected nucleotide, under hybridization conditions to form a hybridization product; (c) performing a primer extension reaction with the hybridization product and a detectably labeled, identified chain-terminating nucleotide under conditions for primer extension; (d) detecting the presence or absence of a label incorporated into the hybridization product, the presence of a label indicating the incorporation of the labeled chain-terminating nucleotide into the hybridization product, and the identity of the incorporated labeled chain-terminating nucleotide indicating the identity of the nucleotide complementary to the selected nucleotide; and (e) comparing the

identity of the selected nucleotide with a non-polymorphic nucleotide, a different identity of the selected nucleotide from that of the non-polymorphic nucleotide indicating a polymorphism of that selected nucleotide."

The Irving et al Reference

The Irving et al reference is United States Patent No. 6,468,330 for a mini-cyclone biocollector and concentrator illustrated in FIG. 1 reproduce below and the portions of the specification quoted below.



As shown in FIGS. 1 and 2, the mini-cyclone particle separator assembly 2 includes base section 10 comprising an internal reservoir 12 and a lower vacuum chambers 14. Referring to FIGS. 1, 2 and 3B, lower vacuum chambers 14 is located toward the top of base section 10 adjacent underfluid or flow pipe outlet 28 of conical cyclone section 20 discussed below. Lower vacuum chambers 14 is connected in fluid or flow communication to four vacuum transfer channels 52 at lower openings 19. Each opening 19 is located adjacent to underfluid or flow pipes 28. Reservoir 12 stores the liquid and provides a collection location to receive liquid from underfluid or flow pipe 28. At the bottom of the base section 10, a small diameter central outlet 16 is provided to connect to the suction side of a peristaltic pump (not shown). The pump, in operation with a solenoid valve, lifts the liquid from internal reservoir 12 upwardly through a central liquid passage 24 of cyclone section 20 and into the top of the cyclone chambers 22. Base section 10 may include an internal shoulder 18 located approximately midway down the height of interior wall of base section 10. Internal shoulder 18 provides support for three screens (not shown) that break up any foam in the liquid stream fluid or flowing out of

underfluid or flow pipe 28. The control unit (not shown) can direct the liquid collected through a conduit attached to outlet 16 to a monitoring system to check for the presence of toxic microorganisms among the particles collected.

The Rejection Does Not Establish a *Prima Facie* Case of Obviousness

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) include, "Ascertaining the differences between the prior art and the claims at issue." The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness (M.P.E.P. Section 2142). Three basic criteria must be met in order for the Examiner to establish a *prima facie* case of obviousness. The prior art reference (or reference when combined) must teach or suggest all the claim limitations. There must be a reasonable expectation of success with the proposed combination. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

Miles, Casey, and Irving Do Not Teach All Claim Limitations

The Miles, Casey, and Irving references do not disclose a number of Applicants' claim limitations. The criteria that the prior art reference, or references when combined, must teach or suggest all the claim limitations has not been met. The Miles reference and the Casey reference and the Irving reference do not disclose the limitations of Applicants' claims 1-4, 12, 27, 29, 31-35, and 40 identified below.

"autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles," or

"a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air," or

"a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles," or

"a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads," or

"wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents," or

"said collector includes a separator for separating said potential bioagent particles from said other particles," or

"means for lysis of said spores," or

"polystyrene beads," or

"said laser unit includes a red laser that classifies said microbeads and a green laser that quantifies said microbeads," or

"said sample preparation means includes optically encoded microbeads and bead suspension/mixer means for suspending said microbeads for a predetermined time period."

Since the limitations listed and described above are not shown by the Miles reference, the Casey reference, or the Irving reference, a *prima facie* case of obviousness has not been established. Further, since the Miles reference and the

Casey reference and the Irving reference fail to show the claim limitations of Applicants' claims 1-4, 12, 27, 29, 31-35, and 40 there can be no combination of the three references that would show Applicant's invention. There is no combination of the Miles reference and the Casey reference and the Irving reference that would produce the combination of elements of Applicants' claims 1-4, 12, 27, 29, 31-35, and 40.

No Reasons for Combining Miles, Casey, and the Irving

The criteria that the Examiner must provide reasons for combining the references has not been established. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

The rejection in the Office Action mailed April 29, 2008 does not provide an explanation of how or why the Miles reference and the Casey reference and the Irving reference would be combined. The Miles reference and the Casey reference and the Irving reference do not recognize the problem solved by Applicant's claimed invention. The Miles reference and the Casey reference and the Irving reference fail to disclose the benefits of Applicants claimed invention wherein "particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected and any bioagents in the collected particles are detected by a detector."

Teaching-Suggestion-Motivation (TSM) Test

The Rejection mailed April 29, 2008 does not meet the teaching-suggestion-motivation (TSM) test. The TSM test is "whether there is something in the prior art to suggest the desirability, and thus the obvious nature, of the combination of the references." The Rejection mailed April 29, 2008 does not

point to anything in the prior art to suggest the desirability, and thus the obvious nature, of the combination of the Miles reference and the Casey reference and the Irving reference. Further there are no "other "reasons" for combining the references.

35 U.S.C. § 103(a) Miles, Casey, and Irving Rejection Should Be Reversed

The combination of references in the Office Action mailed April 29, 2008 fails to support a rejection of claims 1-4, 12, 27, 29, 31-35, and 40 under 35 U.S.C. § 103(a), and the rejection should be reversed.

Argument Relating to Grounds of Rejection #3

The rejection of Appellants' claim 19 under 35 U.S.C. § 103(a) as being unpatentable over Miles in view of Casey and Irving and further in view of Colston does not meet the standard of 35 U.S.C. § 103(a). The Miles, Casey, and Irving references are described above.

The Colston et al Reference

The Colston et al reference is United States Published Patent Application No. 2003/0032172 for an automated nucleic acid assay system illustrated in figure 2 and the portion of specification of the patent reproduced below.

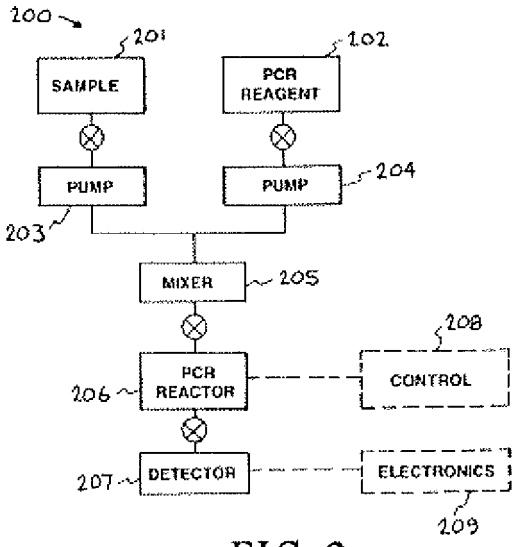


FIG. 2

"The system 200 provides a system capable of performing, singly or in combination, sample preparation, nucleic acid amplification, and nucleic acid detection functions. The nucleic acid assay system 200 includes a number components. A sample is contained in unit 201. A PCR reagent is contained in unit 202. A pump 203 transfers the sample from unit 201 into mixer 205. A pump 204 transfers the PCR reagent from unit 202 into mixer 205. The mixer 205 combines the sample and the PCR reagent. In one embodiment the PCR reagent includes primers. In another embodiment the PCR reagent includes oligos. The mixer 205 can be, for example, a super serpentine reactor, available from Global FIA, Inc, Fox Island, Wash. The mixed sample and reagent are transferred to a PCR reactor 206. This results in an amplified sample. In one embodiment the PCR reactor 206 includes an embedded thermocouple calibration conduit. PCR amplification devices are described in publications such as U.S. Pat. No. 5,589,136 for silicon-based sleeve devices for chemical reactions, assigned to the Regents of the University of California, inventors: M. Allen Northrup, Raymond P. Mariella, Jr., Anthony V. Carrano, and Joseph W. Balch, patented Dec. 31, 1996 and many are commercially available such as ABI PRISM® 7700 Sequence Detection System by Applied Biosystems; iCycler iQ Real-Time PCR Detection System by Bio-Rad; and Smart Cycler® System by Cepheid. The amplified sample is transferred from the PCR reactor 206 detector 207. The detector can be, for example, a detection system described in publications and products produced by Cepheid and Baltimore-based Environmental Technologies Group, Inc. (ETG), a part of London-based Smiths Aerospace."

The Rejection Does Not Establish a *Prima Facie* Case of Obviousness

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) include, "Ascertaining the differences between the prior art and the claims at issue." The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness (M.P.E.P. Section 2142). Three basic criteria must be met in order for the Examiner to establish a *prima facie* case of obviousness. The prior art reference (or reference when combined) must teach or suggest all the claim limitations. There must be a reasonable expectation of success with the proposed combination. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

Miles, Casey, Irving, and Colston Do Not Teach All Claim Limitations

The Miles, Casey, Irving, and Colston references do not disclose a number of Applicants' claim limitations. The criteria that the prior art reference, or references when combined, must teach or suggest all the claim limitations has not been met. The Colston reference and the Casey reference and the Irving reference do not disclose the limitations of Applicants' claim 19 identified below.

> "a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air," or
>
> "a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange

fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles," or

"a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads," or

"wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents," or

"wherein said wetted wall sample preparer includes a super serpentine reactor."

Since the limitations listed and described above are not shown by the Miles, Casey, Irving, and Colston references, a *prima facie* case of obviousness has not been established. Further, since the Miles, Casey, Irving, and Colston references fail to show the claim limitations of Applicants' claim 19 there can be no combination of the four references that would show Applicant's invention. There is no combination of the Miles, Casey, Irving, and Colston references that would produce the combination of elements of Applicants' claim 19. Thus, the combination of references in the Office Action mailed April 29, 2008 fails to support a rejection of claim 19 under 35 U.S.C. § 103(a), and the rejection should be reversed.

No Reasons for Combining Miles, Casey, Irving, and Colston

The criteria that the Examiner must provide reasons for combining the references has not been established. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the

requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

The rejection in the Office Action mailed April 29, 2008 does not provide an explanation of how or why the Miles, Casey, Irving, and Colston references would be combined. The Miles, Casey, Irving, and Colston references do not recognize the problem solved by Applicant's claimed invention. The Miles, Casey, Irving, and Colston references fail to disclose the benefits of Applicants claimed invention wherein "particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected and any bioagents in the collected particles are detected by a detector."

Teaching-Suggestion-Motivation (TSM) Test

The Rejection mailed April 29, 2008 does not meet the teaching-suggestion-motivation (TSM) test. The TSM test is "whether there is something in the prior art to suggest the desirability, and thus the obvious nature, of the combination of the references." The Rejection mailed April 29, 2008 does not point to anything in the prior art to suggest the desirability, and thus the obvious nature, of the combination of the Miles, Casey, Irving, and Colston references. Further there are no "other "reasons" for combining the references.

Miles, Casey, Irving, and Colston Rejection Should Be Reversed

The combination of references in the Office Action mailed April 29, 2008 fails to support a rejection of claim 19 under 35 U.S.C. § 103(a), and the rejection should be reversed.

Argument Relating to Grounds of Rejection #4

The rejection of Appellants' claims 1-5, 29, 32, 33, and 35-37 as being obvious over Daugherty et al. U.S. Published Patent Application No. 2004/0028561 (hereinafter "Daugherty") in view of Casey and Irving does not

meet the standard of 35 U.S.C. § 103(a). The Casey and Irving references are described above.

The Daugherty Reference

The Daugherty et al reference is United States Published Patent Application No. 2004/0028561 for a system for the detection of pathogens in the mail stream illustrated in figure 6B and the portion of specification of the patent reproduced below.

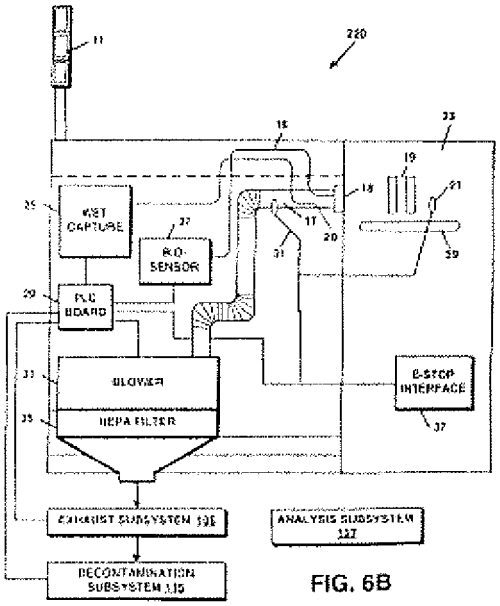


FIG. 6B

"Referring now to FIGS. 6A and 6B, system 220, in which the illustrative embodiment of the control flow 220 for mail sortation is shown. As mail pieces are fed into system 220, through feeder 41, particles are released through normal handling and/or through pinch point pulley assembly 19. Particles are moved through prefilter 18 which allows large particles to pass through the prefilter 18 and exhaust back into the blower/air filtration system 33/35 through simplified hoodless ducting 17 as waste air. Smaller particles enter pitot tube entry 20, into the region in which the particles are tested for contamination. In the illustrative embodiment, the region includes sampling subsystem 123 and triggering subsystem 119 (shown in FIG. 1), embodied in wet capture 25 and biosensor 27/indicator light 11 respectively. After the mail parcels have been fed into the system, they proceed through closed vent/hood 23 on mail transport device 39 towards mail stacker 43 which is enclosed by open vent/hood 45. In general, conventional closed and open vent/hoods 23 and 45, respectively, are custom-fitted to all types of mail transport equipment (i.e. mail transport equipment manufactured

by Lockheed Martin, Pitney-Bowes, Bell & Howell, Siemans, etc.) and conventional mail sortation stacker sections 43, pockets, or sort bin destinations typically installed at mail processing facilities as well as commercial pre-sort facilities and mailrooms."

Appellants Disagree with Examiner's Finding of Fact – Daugherty

The Appellants disagree with the Examiner's Finding of Fact regarding the Daugherty reference. The Rejection mailed April 29, 2008 states: "Daugherty et at. fail to teach a detector comoprising a flow cytometer for use with optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads, each with a unique spectral address and coated with capture antibodies specific for a given antigen, and also fails to teach an aerosol collector that is a wetted wall cyclone collector that concentrates said potential bioagent particles in a liquid."

Appellants point out that there are other claim limitations that are not taught by the Daugherty reference. The Daugherty reference does not show Appellants' "autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles." The Daugherty reference only shows a "system for the detection of pathogens in the mail stream." The Daugherty reference does not show an autonomous monitoring apparatus for monitoring air for bioagents.

The Daugherty reference does not show Appellants' "collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air." The Daugherty reference only shows a "system for the detection of pathogens in the mail stream." The Daugherty reference does not show a collector separating selected potential bioagent particles from air.

The Daugherty reference does not show Appellants' "wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said

wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid." The Daugherty reference only shows a "system for the detection of pathogens in the mail stream." The Daugherty reference does not show a "wetted wall sample preparer" or a "wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector" or a "wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid."

The Daugherty reference does not show Appellants' "detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads." The Daugherty reference only shows "system for the detection of pathogens in the mail stream." The Daugherty reference does not show a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads.

The Daugherty reference does not show Appellants' "flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents." The Daugherty reference only shows a "system for the detection of pathogens in the mail stream." The Daugherty reference does not show a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange

fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents.

The Rejection Does Not Establish a *Prima Facie* Case of Obviousness

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) include, "Ascertaining the differences between the prior art and the claims at issue." The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness (M.P.E.P. Section 2142). Three basic criteria must be met in order for the Examiner to establish a *prima facie* case of obviousness. The prior art reference (or reference when combined) must teach or suggest all the claim limitations. There must be a reasonable expectation of success with the proposed combination. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

Daugherty, Casey, and Irving Do Not Teach All Claim Limitations

The Daugherty, Casey, and Irving references do not disclose a number of Applicants' claim limitations. The criteria that the prior art reference, or references when combined, must teach or suggest all the claim limitations has not been met. The Daugherty, Casey, and Irving references do not disclose the limitations of Applicants' claims 1-5, 29, 32, 33, and 35-37 identified below.

> "autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles," or

"a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air," or

"a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles," or

"a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads," or

"wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents," or

"wherein said collector is an aerosol collector," or

"said collector includes a separator for separating said potential bioagent particles from said other particles," or

"wherein said collector is an aerosol collector that collects air and includes means for separating said air into a bypass air flow that does not contain said potential bioagent particles of a predetermined particle size range and a product air flow that contains said potential bioagent particles of a predetermined particle size range." Or

"means for lysis of said spores," or

"wherein said confirmation means is a multiplex PCR detector," or

"wherein said confirmation means is a real time PCR detector," or

"wherein said confirmation means includes means for performing PCR amplification."

Since the limitations listed and described above are not shown by the Daugherty, Casey, and Irving references, a *prima facie* case of obviousness has not been established. Further, since the Daugherty, Casey, and Irving references fail to show the claim limitations of Applicants' claims 1-5, 29, 32, 33, and 35-37 there can be no combination of the three references that would show Applicant's invention. There is no combination of the Daugherty, Casey, and Irving references that would produce the combination of elements of Applicants' claims 1-5, 29, 32, 33, and 35-37. Thus, the combination of references in the Office Action mailed April 29, 2008 fails to support a rejection of claims 1-5, 29, 32, 33, and 35-37 under 35 U.S.C. § 103(a), and the rejection should be reversed.

No Reasons for Combining Daugherty, Casey, and Irving

The criteria that the Examiner must provide reasons for combining the references has not been established. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

The rejection in the Office Action mailed April 29, 2008 does not provide an explanation of how or why the Daugherty, Casey, and Irving references would be combined. The Daugherty, Casey, and Irving references do not recognize the problem solved by Applicant's claimed invention. The Daugherty, Casey, and Irving references fail to disclose the benefits of Applicants claimed invention wherein "particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected and any bioagents in the collected particles are detected by a detector." Thus, the combination of

references in the Office Action mailed April 29, 2008 fails to support a rejection of claims 1-5, 29, 32, 33, and 35-37 under 35 U.S.C. § 103(a), and the rejection should be reversed.

Teaching-Suggestion-Motivation (TSM) Test

The Rejection mailed April 29, 2008 does not meet the teaching-suggestion-motivation (TSM) test. The TSM test is "whether there is something in the prior art to suggest the desirability, and thus the obvious nature, of the combination of the references." The Rejection mailed April 29, 2008 does not point to anything in the prior art to suggest the desirability, and thus the obvious nature, of the combination of the Daugherty, Casey, and Irving. Further there are no "other "reasons" for combining the references. Thus, the combination of references in the Office Action mailed April 29, 2008 fails to support a rejection of claims 1-5, 29, 32, 33, and 35-37 under 35 U.S.C. § 103(a), and the rejection should be reversed.

SUMMARY

The present invention provides an autonomous monitoring apparatus for monitoring air for bioagents. Bioagents in the collected particles are detected by a detector system. Small diameter polystyrene beads are coded with 1000s of antibodies. The sample is first exposed to the beads and the bioagent, if present, is bound to the bead. A second, fluorescently labeled antibody is then added to the sample resulting in a highly fluorescent target for flow analysis. Each microbead is colored with a unique combination of red and orange emitting dyes. The number of agents that can be detected from a single sample is limited only by the number of colored bead sets. None of the cited references discloses Appellants' claimed invention.

There could be no combination of the references that would support a 35 U. S. C §103(a) rejection of Appellants' claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 and the rejection should be reversed.

It is respectfully requested that claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 on appeal be allowed.

Respectfully submitted,

By: _____

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Date: August 15, 2008

VIII. CLAIMS APPENDIX

1. An autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles, comprising:

a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air;

a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles; and

a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads and

wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents.

2. The apparatus of claim 1 wherein said collector is an aerosol collector.

3. The apparatus of claim 1 wherein said air includes other particles in addition to said potential bioagent particles and wherein said collector includes a

separator for separating said potential bioagent particles from said other particles.

4. The apparatus of claim 3 wherein said potential bioagent particles are of a predetermined size range and said separator separates said potential bioagent particles are of a predetermined size range from said other particles.

5. The apparatus of claim 4 wherein said collector is an aerosol collector that collects air and includes means for separating said air into a bypass air flow that does not contain said potential bioagent particles of a predetermined particle size range and a product air flow that contains said potential bioagent particles of a predetermined particle size range.

12. The apparatus of claim 1 wherein said potential bioagent particles contain spores and including means for lysis of said spores.

15. The apparatus of claim 1 wherein said wetted wall sample preparer includes a sequential injection analysis system.

16. The apparatus of claim 1 wherein said wetted wall sample preparer includes a flow injection analysis system.

19. The apparatus of claim 1 wherein said wetted wall sample preparer includes a super serpentine reactor.

27. The apparatus of claim 1 wherein said optically encoded microbeads are polystyrene beads.

29. The apparatus of claim 1 wherein said flow cytometer for analyzing said optically encoded microbeads with said laser unit includes a red laser that classifies said microbeads and a green laser that quantifies said microbeads.

31. The apparatus of claim 1 wherein said detector includes a liquid-array based multiplex immunoassay detector.

32. The apparatus of claim 1 wherein said detector includes a multiplex PCR detector.

33. The apparatus of claim 1 including confirmation means for confirming said bioagents in said sample.

34. The apparatus of claim 33 wherein said confirmation means is a multiplex immunoassay detector.

35. The apparatus of claim 33 wherein said confirmation means is a multiplex PCR detector.

36. The apparatus of claim 33 wherein said confirmation means is a real time PCR detector.

37. The apparatus of claim 33 wherein said confirmation means includes means for performing PCR amplification.

38. The apparatus of claim 33 wherein said confirmation means includes means for injecting/aspirating a sample, means for adding PCR reagent, means for mixing sample and reagent, means for transport to PCR reactor, means for performing PCR amplification, means for transport of amplified sample from PCR reactor, and means for detection of PCR amplicon.

39. The apparatus of claim 33 wherein said confirmation means includes means for injecting/aspirating a sample, means for adding PCR reagent, means for mixing sample and reagent, means for transport to PCR reactor, means for performing PCR amplification, means for transport of amplified sample from PCR reactor, means for detection of PCR amplicon, and means for decontamination and conditioning of all exposed conduits.

40. The apparatus of claim 1 wherein said sample preparation means includes optically encoded microbeads and bead suspension/mixer means for suspending said microbeads for a predetermined time period.

IX. EVIDENCE APPENDIX

1. *Wikipedia, the free encyclopedia* description of the Lawrence Livermore National Laboratory

X. RELATED PROCEEDINGS APPENDIX

There are no entries in the Related Proceedings Appendix.

Lawrence Livermore National Laboratory

From Wikipedia, the free encyclopedia

The **Lawrence Livermore National Laboratory (LLNL)** in Livermore, California is a United States Department of Energy (DOE) national laboratory, managed and operated by Lawrence Livermore National Security, LLC (LLNS), a partnership of Bechtel National, the University of California, Babcock and Wilcox, Washington Division of URS Corporation, and Battelle; the Texas A&M University System is also an affiliate of LLNS. On October 1, 2007 LLNS assumed management of LLNL from the University of California, which had managed and operated the Laboratory since its inception in 1952.

Lawrence Livermore National Laboratory

University of California

Lawrence Livermore National Laboratory

Motto	"Science in the national interest"
Established	1952 by the University of California
Research Type	National security, nuclear science
Budget	US$1.6 billion
Director	George H. Miller
Staff	6,800
Location	Livermore, California
Campus	3.2 km² (800 acres)
Operating Agency	Lawrence Livermore National Security, LLC
Website	www.llnl.gov (http://www.llnl.gov/)

Contents

Background

LLNL is self-described as "a premier research and development institution for science and technology applied to national security."[1] Its principal responsibility is ensuring the safety, security and reliability of the nation's nuclear weapons through the application of advanced science, engineering and technology. The Laboratory also applies its special expertise and multidisciplinary capabilities to preventing the proliferation and use of weapons of mass destruction, bolstering homeland security and solving other nationally important problems, including energy and environmental security, basic science and economic competitiveness.

LLNL is home to many unique facilities and a number of the most powerful computer systems in the world, according to the TOP500 list, including Blue Gene/L, the world's fastest computer from 2004 until Los Alamos National Laboratory's Roadrunner supercomputer surpassed it in 2008. The Lab is a leader in technical innovation: since 1978, LLNL has received a total of 118 prestigious R&D 100 Awards, including five in 2007. [2] The awards are given annually by the editors of *R&D Magazine* to the most innovative ideas of the year.

The Laboratory is located on a one-square-mile (2.6-km2) site at the eastern edge of Livermore, California. It also operates a 7000-acre remote experimental test site, called Site 300, situated about 15 miles (24 km) southeast of the main Lab site. LLNL has an annual budget of about US$1.5 billion and a staff of roughly 7,000 employees.

Origins

LLNL was established in 1952 to spur innovation and provide competition to the nuclear weapon design laboratory at Los Alamos, New Mexico, home of the Manhattan Project that developed the first atomic weapons. Edward Teller and Ernest O. Lawrence, director of the University of California Radiation Laboratory at Berkeley, are regarded as the co-founders of the Livermore Laboratory.

The new laboratory was sited was at a former Naval Air Base and training station in Livermore, California. The site was already home to several University of California Radiation Laboratory projects that were too large for its location in the hills above the Berkeley campus, including one of the first experiments in the magnetic approach to confined thermonuclear reactions (i.e., fusion).

E.O. Lawrence tapped 32-year-old Herbert York, a former graduate student of his, to run the Livermore Laboratory. Under York, the Lab had four main programs: Project Sherwood (the Magnetic Fusion Program), Project Whitney (the weapons design program), diagnostic weapon experiments (both for the Los Alamos and Livermore laboratories) and a basic physics program. York also saw to it that the new lab embraced the E.O. Lawrence "big science" approach, tackling challenging projects with physicists, chemists, engineers, and computational scientists working together in multidisciplinary teams.

Historically, the Berkeley and Livermore laboratories have had very close relationships on research projects, business operations and staff. The Livermore Lab was established initially as a branch of the Berkeley Laboratory. Both labs are named after E.O. Lawrence, and the Livermore Lab was not officially severed administratively from the Berkeley Lab until the early 1970s. To this day, in official planning documents and records, Lawrence Berkeley National Laboratory is designated as Site 100, Lawrence Livermore National Lab as Site 200, and LLNL's remote test location as Site 300. [3]

Weapons projects

From its inception, Livermore focused on innovative weapon design concepts; as a result, its first three nuclear tests were unsuccessful. However, the Lab persevered and its subsequent designs proved increasingly successful. In 1957, the Livermore Lab was selected to develop the warhead for the Navy's Polaris missile. This warhead required numerous innovations to fit a nuclear warhead into the relatively small confines of the missile nosecone.[4]

During the decades of the Cold War, more than a score of Livermore-designed warheads entered the nation's nuclear stockpile, ranging in size from the Lance surface-to-air tactical missile to the megaton-class Spartan antiballistic missile warhead. Over the years, LLNL designed the following warheads: W27 (Regulus cruise missile; 1955; joint with Los Alamos), W38 (Atlas/Titan ICBM; 1959), B41 (B52 bomb; 1957), W45 (Little John/Terrier missiles; 1956), W47 (Polaris SLBM; 1957), W48 (155-mm howitzer; 1957), W55 (submarine rocket; 1959), W56 (Minuteman ICBM; 1960), W58 (Polaris SLBM; 1960), W62 (Minuteman ICBM; 1964), W68 (Poseidon SLBM; 1966), W70 (Lance missile; 1969), W71 (Spartan missile; 1968), W79 (8-in. artillery gun; 1975), W82 (155-mm howitzer; 1978), B83 (modern strategic bomb; 1979), W87 (Peacekeeper/MX ICBM; 1982), and W89 (Tomahawk GLCM; 1978). The W87 and the B83 are the only LLNL designs still in the U.S. nuclear stockpile. [5][6][7]

With the collapse of the Soviet Union and the end of the Cold War, the United States began a moratorium on nuclear testing and development of new nuclear weapon designs. To sustain existing warheads for the indefinite future, a science-based Stockpile Stewardship Program (SSP) was defined that emphasized the development and application of greatly improved technical capabilities to assess the safety, security, and reliability of existing nuclear warheads without the use of nuclear testing. Confidence in the performance of weapons, without nuclear testing, is maintained through an ongoing process of stockpile surveillance, assessment and certification, and refurbishment or weapon replacement.

With no new designs of nuclear weapons, the warheads in the U.S. stockpile must continue to function far past their original expected lifetimes. As components and materials age, problems can arise. Stockpile Life Extension Programs can extend system lifetimes, but they also can introduce performance uncertainties and require maintenance of outdated technologies and materials. Because there is concern that it will become increasingly difficult to maintain high confidence in the current warheads for the long term, the Department of Energy/National Nuclear Security Administration initiated the Reliable Replacement Warhead (RRW) Program. RRW designs could reduce uncertainties, ease maintenance demands, and enhance safety and security. In March 2007, the LLNL design was chosen for the Reliable Replacement Warhead. [8] Since that time, however, Congress has not allocated funding for any further development of the RRW.

Plutonium research

LLNL conducts research into the properties and behavior of plutonium to learn how plutonium performs as it ages and how it behaves under high pressure (e.g., with the impact of high explosives). Plutonium is a complex and perplexing element. For instance, it has seven temperature-dependent solid phases—more than any other element in the periodic table. Each phase possesses a different density and volume and has its own characteristics. Alloys of plutonium are even more complex; multiple phases can be present in a sample at any given time. Experiments are being conducted at LLNL and elsewhere to measure the structural, electrical and chemical properties of plutonium and its alloys and to determine how these materials change over time. Such measurements will enable scientists to better model and predict plutonium's long-term behavior in the aging stockpile. [9]

The Lab's plutonium research is conducted in a specially designed, ultra-safe, and highly secure facility called the SuperBlock. Work with highly enriched uranium is also conducted here. In March 2008, the National Nuclear Security Administration presented its preferred alternative for the transformation of the nation's nuclear weapons complex. Under this plan, LLNL would be a center of excellence for nuclear design and engineering, a center of excellence for high explosive research and development, and a science magnet in high-energy-density (i.e., laser) physics. In addition, most of its special nuclear material would be removed and consolidated at a more central, yet-to-be-named site. [10]

National Ignition Facility and photon science

- National Ignition Facility (NIF)  37.690555, -121.700555 (http://stable.toolserver.org/geohack/geohack.php?pagename=Lawrence_Livermore_National_Laboratory&params=37.690555_N_-121.700555_E_) is a laser-based inertial confinement fusion (ICF) research facility under construction at the Livermore Lab. NIF uses powerful lasers to heat and compress a small amount of hydrogen fuel to the point where nuclear fusion reactions take place. NIF is the largest and most energetic ICF device built to date, and the first that is expected to reach the long-sought goal of "ignition," when the fusion reactions become self-sustaining.[11]

The National Ignition Facility (NIF) Project and related programs -- the National Ignition Campaign, Photon Science and Applications, Inertial Fusion Energy and Science at the Extremes -- are pursuing three complementary missions:

- **National security**: To ensure the continuing reliability of the U.S. nuclear stockpile, Lawrence Livermore and other national laboratories are developing sophisticated supercomputer simulations to determine the effects of aging on nuclear weapons components as part of the national Stockpile Stewardship Program. When NIF is completed, it will be able to provide data for these simulations by replicating the conditions that exist inside a thermonuclear weapon. In addition, the Photon Science and Applications program is developing innovative technologies for homeland security and national defense.

- **Energy for the future**: By demonstrating the ability to attain fusion ignition in the laboratory, NIF will lay the groundwork for future decisions about fusion's long-term potential as a safe, virtually unlimited energy source. Fusion, the same energy source that powers the stars, produces no greenhouse gases and is more environmentally benign than fossil-fuel- or nuclear-fission-based energy.

- **Understanding the universe**: NIF's role in the physics of materials under extreme pressures and temperatures, known as high-energy-density physics, is key to unlocking the secrets of the universe. Other NIF programs promise breakthroughs in the use of lasers in medicine, radioactive and hazardous waste treatment, particle physics, and x-ray and neutron science.

Global security program

The Lab's work in global security aims to reduce and mitigate the dangers posed by the spread or use of weapons of mass destruction and by threats to energy and environmental security. Livermore has been working on global security and homeland security for decades, predating both the collapse of the Soviet Union in 1991 and the September 11, 2001, terrorist attacks. LLNL staff have been heavily involved in the cooperative nonproliferation programs with Russia to secure at-risk weapons materials and assist former weapons workers in developing peaceful applications and self-sustaining job

opportunities for their expertise and technologies. In the mid-1990s, Lab scientists began efforts to devise improved biodetection capabilities, leading to miniaturized and autonomous instruments that can detect biothreat agents in a few minutes instead of the days to weeks previously required for DNA analysis.

Today, Livermore researchers address the full spectrum of threats – radiological/nuclear, chemical, biological, explosives, and cyber. They combine physical and life sciences, engineering, computations, and analysis to develop technologies that solve real-world problems. Activities are grouped into five programs:

- **Nonproliferation**. Preventing the spread of materials, technology and expertise related to weapons of mass destruction (WMD) and detecting WMD proliferation activities worldwide.
- **Domestic security**: Anticipating, innovating and delivering technological solutions to prevent and mitigate devastating high-leverage attacks on U.S. soil.
- **Defense**: Developing and demonstrating new concepts and capabilities to help the Department of Defense prevent and deter harm to the nation, its citizens and its military forces.
- **Intelligence**: Working at the intersection of science, technology and analysis to provide insight into the threats to national security posed by foreign entities.
- **Energy and environmental security**: Furnishing scientific understanding and technological expertise to devise energy and environmental solutions at global, regional and local scales.

Other programs

LLNL supports capabilities in a broad range of scientific and technical disciplines, applying current capabilities to existing programs and developing new science and technologies to meet future national needs.

- The Lab's chemistry, materials, and life science research focuses on chemical engineering, nuclear chemistry, materials science, and biology and bio-nanotechnology.
- Physics thrust areas include condensed matter and high-pressure physics, optical science and high-energy-density physics, medical physics and biophysics, and nuclear particle and accelerator physics.
- In the area of energy and environmental science, Livermore's emphasis is on carbon and climate, energy, water and the environment, and the national nuclear waste repository.
- LLNL engineering activities include micro- and nanotechnology, lasers and optics, biotechnology, precision engineering, nondestructive characterization, modeling and simulation, systems and decision science, and sensors, imaging and communications.
- The Lab is a world leader in computer science, with thrust areas in computing applications and research, integrated computing and communications systems, and cyber security.

Key accomplishments

Over its 55-year history, Lawrence Livermore has made many scientific and technological achievements, including [12]:

- Critical contributions to the U.S. nuclear deterrence through the design of nuclear weapons to meet military requirements and, since the mid-1990s, through the Stockpile Stewardship Program, by which the safety and reliability of the enduring stockpile is ensured without underground nuclear testing.
- Design, construction, and operation of a series of ever larger, more powerful, and more capable laser systems, culminating in the 192-beam National Ignition Facility (NIF), scheduled for completion in 2009.
- Advances in accelerator and fusion technology, including magnetic fusion, free-electron lasers, accelerator mass spectrometry, and inertial confinement fusion.
- Breakthroughs in high-performance computing, including the development of novel concepts for massively parallel computing and the design and application of computers that can carry out hundreds of trillions of operations per second.
- Development of technologies and systems for detecting nuclear, radiological, chemical, biological, and explosive threats to prevent and mitigate WMD proliferation and terrorism.
- Development of extreme-ultraviolet lithography (EUVL) for fabricating next-generation computer chips.
- First-ever detection of massive compact halo objects (MACHOs), a suspected but previously undetected component of dark matter.
- Advances in genomics, biotechnology, and biodetection, including major contributions to the complete sequencing of the human genome though the Joint Genome Institute and the development of rapid PCR (polymerase chain reaction)

technology that lies at the heart of today's most advanced DNA detection instruments.
- Development and operation of the National Atmospheric Release Advisory Center (NARAC), which provides real-time, multi-scale (global, regional, local, urban) modeling of hazardous materials released into the atmosphere.
- Development of highest resolution global climate models and contributions to the International Panel on Climate Change which, together with former vice president Al Gore, was awarded the 2007 Nobel Peace Prize.
- Co-discoverers of new superheavy elements 113, 114, 115, 116, and 118.
- Invention of new healthcare technologies, including a microelectrode array for construction of an artificial retina, a miniature glucose sensor for the treatment of diabetes, and a compact proton therapy system for radiation therapy.

Unique facilities

- Biosecurity and Nanoscience Laboratory. Researchers apply advances in nanoscience to develop novel technologies for the detection, identification, and characterization of harmful biological pathogens (viruses, spores, and bacteria) and chemical toxins.

- Center for Accelerator Mass Spectrometry: LLNL's Center for Accelerator Mass Spectrometry (CAMS) develops and applies a wide range of isotopic and ion-beam analytical tools used in basic research and technology development, addressing a spectrum of scientific needs important to the Laboratory, the university community, and the nation. CAMS is the world's most versatile and productive accelerator mass spectrometry facility, performing more than 25,000 AMS measurement operations per year.

- High Explosives Applications Center and Energetic Materials Center: At HEAF, teams of scientists, engineers, and technicians address nearly all aspects of high explosives: research, development and testing, material characterization, and performance and safety tests. HEAF activities support the Laboratory's Energetic Materials Center, a national resource for research and development of explosives, pyrotechnics, and propellants.

- National Atmospheric Release Advisory Center: NARAC is a national support and resource center for planning, real-time assessment, emergency response, and detailed studies of incidents involving a wide variety of hazards, including nuclear, radiological, chemical, biological, and natural atmospheric emissions.

- National Ignition Facility: This 192-beam, stadium-size laser system will be used to compress fusion targets to conditions required for thermonuclear burn. Experiments at NIF will study physical processes at conditions that exist only in the interior of stars and in exploding nuclear weapons (see National Ignition Facility and photon science, above).

- Superblock: This unique facility houses modern equipment for research and engineering testing of nuclear materials and is the place where plutonium expertise is developed, nurtured, and applied. Research on highly enriched uranium also is performed here.

- Terascale Simulation Facility: LLNL's Terascale Simulation Facility houses two of the world's most powerful computers, ASC Purple and BlueGene/L. BlueGene/L has occupied the No. 1 position on the Top500 list since November 2004; the current system achieves a Linpack benchmark performance of 478.2 TFlop/s (teraflops, or trillions of calculations per second).

- Titan Laser. Titan is a combined nanosecond-long pulse and ultrashort-pulse (subpicosecond) laser, with hundreds of joules of energy in each beam. This petawatt-class laser is used for a range of high-energy-density physics experiments, including the science of fast ignition for inertial confinement fusion energy.

World-class computers

Throughout its history, LLNL has been a leader in computers and scientific computing. Even before the Livermore Lab opened its doors, E.O. Lawrence and Edward Teller recognized the importance of computing and the potential of computational simulation. Their purchase of one of the first UNIVAC computers, set the precedent for LLNL's history of acquiring and exploiting the fastest and most capable supercomputers in the world. A succession of increasingly powerful and fast computers have been used at the Lab over the years:

- 1953 Remington-Rand UNIVAC I (Universal Automatic Computer)
- 1954 IBM 701
- 1956 IBM 704
- 1958 IBM 709
- 1960 IBM 7090
- 1960 Remington-Rand LARC (Livermore Advanced Research Computer)
- 1961 IBM 7030 (Stretch)
- 1963 IBM 7094
- 1963 CDC 1604
- 1963 CDC 3600
- 1964 CDC 6600
- 1969 CDC 7600
- 1974 CDC STAR 100
- 1978 Cray-1
- 1984 Cray X-MP
- 1985 Cray-2
- 1989 Cray Y-MP
- 1992 BBN Butterfly
- 1994 Meiko CS-2
- 1995 [[Cray C9[0]]
- 1995 Cray T3D
- 1998 IBM ASCI Blue Pacific
- 2000 IBM ASCI White
- 2005 IBM Blue Gene/L
- 2004 Thunder
- 2005 ASC Purple
- 2006 Zeus
- 2006 Rhea
- 2006 Atlas
- 2007 Minos

The November 2007 release of the 30th TOP500 list of the 500 most powerful computer systems in the world, has LLNL's BlueGene/L computer in first place for the seventh consecutive time. Five other LLNL computers are in the top 100.

On June 22, 2006, researchers at LLNL announced that they had devised a scientific software application that sustained 207.3 trillion operations per second. This was the equivalent of an online game capable of handling 300 million simultaneous players. The record performance was made at LLNL on BlueGene/L, the world's fastest supercomputer with 131,072 processors. The record was a milestone in the evolution of predictive science, a field in which researchers use supercomputers to answer questions about such subjects as: materials science simulations, global warming, and reactions to natural disasters.

LLNL has a long history of developing computing software and systems. Initially, there was no commercially available software, and computer manufacturers considered it the customer's responsibility to develop their own. Users of the early computers had to write not only the codes to solve their technical problems, but also the routines to run the machines themselves. Today, LLNL computer scientists focus on creating the highly complex physics models, visualization codes, and other unique applications tailored to specific research requirements. A great deal of software also has been written by LLNL personnel to optimize the operation and management of the computer systems, including operating system extensions such as CHAOS (Linux Clustering) and resource management packages such as SLURM. [13] The Peloton procurements in late 2006 (Atlas and other computers) were the first in which a commercial resource management package, Moab, was used to manage the clusters. [14]

Sponsors

LLNL's principal sponsor is the Department of Energy/National Nuclear Security Administration (DOE/NNSA) Office of Defense Programs, which supports its stockpile stewardship and advanced scientific computing programs. Funding to support LLNL's global security and homeland security work comes from the DOE/NNSA Office of Defense Nuclear Nonproliferation as well as the Department of Homeland Security. LLNL also receives funding from DOE's Office of Science, Office of Civilian Radioactive Waste Management, and Office of Nuclear Energy. In addition, LLNL conducts

work-for-others research and development for various Defense Department sponsors, other federal agencies, including NASA, Nuclear Regulatory Commission (NRC), National Institutes of Health, and Environmental Protection Agency, a number of California State agencies, and private industry.

Directors

The LLNL Director is appointed by the Board of Governors of Lawrence Livermore National Security, LLC (LLNS) and reports to the board. The Laboratory Director also serves as the President of LLNS. Over the course of its 55 year history, ten eminent scientists have served as LLNL Director:

- 1952-1958 Herbert York
- 1958-1960 Edward Teller
- 1960-1961 Harold Brown
- 1961-1965 John S. Foster
- 1965-1971 Michael M. May
- 1971-1988 Roger E. Batzel
- 1988-1994 John H. Nuckolls
- 1994-2002 C. Bruce Tarter
- 2002-2006 Michael R. Anastasio
- 2006-*present* George H. Miller

Organization

The LLNL Director is supported by a senior executive team consisting of the Deputy Director, Principal Associate Directors, Director of Security, and Director of Environment, Safety, Health, and Quality. The organizations of the Laboratory Counsel, Audit and Oversight, Chief Financial Officer, and Contractor Assurance also report to the Laboratory Director.

The Lab is organized into five principal directorates:

- Science and technology
  - Chemistry, materials, earth and life science
  - Physical science
  - Computation and simulations
  - Engineering
- Global security
  - Nonproliferation
  - Domestic security
  - Defense
  - Intelligence
  - Energy and environmental security
- Weapons and complex integration
  - Primary nuclear design
  - Secondary nuclear design
  - Nuclear weapon engineering
  - Advanced simulations and computation
- National Ignition Facility and photon science
  - Inertial confinement fusion energy
  - National Ignition Facility
  - Target experimental systems
  - Photon science and applications
- Operations and business
  - Strategic human capital management
  - Business
  - Facilities and infrastructure
  - Nuclear operations

Footnotes

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- *Preparing for the 21st Century: 40 Years of Excellence*. **Lawrence Livermore National Laboratory**. Report UCRL-AR-108618. 1992.

External links and sources

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- Lawrence Livermore National Security, a Limited Liability Corporation (http://www.llnsllc.com/) (official website)
- Laboratory History (http://www.llnl.gov/50th_anniv/history.htm) (official website)
- LLNL Industrial Partnerships and Commercialization (IPAC) (http://www.llnl.gov/IPandC) (official website)
- University of California Office of Laboratory Management (http://labs.ucop.edu/) (official website)
- Society of Professionals, Scientists and Engineers (http://www.spse.org/) (Union representing UC Scientists and Engineers at LLNL)
- Annotated bibliography for Livermore from the Alsos Digital Library for Nuclear Issues (http://alsos.wlu.edu/qsearch.aspx?browse=places/Livermore,+California)

- Lawrence Livermore National Laboratory is at coordinates 37.686024, -121.709547 (http://stable.toolserver.org/geohack/geohack.php?pagename=Lawrence_Livermore_National_Laboratory&params=37.686024_N_-121.709547_E_type:landmark_region:US&title=Lawrence+Livermore+National+Laboratory)Coordinates: 37.686024, -121.709547 (http://stable.toolserver.org/geohack/geohack.php?pagename=Lawrence_Livermore_National_Laboratory&params=37.686024_N_-121.709547_E_type:landmark_region:US&title=Lawrence+Livermore+National+Laboratory)

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